

Claim Amendments

Applicants have canceled claim 26 and 27 to expedite prosecution. Applicants reserve the right to pursue the cancelled subject matter in applications claiming priority from the instant application. Applicants have amended claim 24 to recite a method comprising the step of administering the compound of the invention to a subject wherein "the subject has been exposed to a promoter of cardiac fibrosis and the step of administering the compound is before the subject exhibits a cardiac fibrotic condition". Original support for this amendment is found throughout the original application, see e.g., p.16, lines 7 - page 17, line 16, as discussed further below. In addition, original support for prevention of cardiac fibrosis and administration of the compound to the subject before the fibrotic process is exhibited is found at p.13, lines 10-14 and p. 27, lines 17-19 and line 22. Thus the amendment adds no new matter.

Applicants have also added claim 28 to more clearly set forth the subject matter of the claimed invention. Claim 28, which depends from claim 24,

specifies that one of the promoters of cardiac fibrosis in claim 24 is elevated angiotensin II. Support for this claim is found in the original application at p.27, line 22 and thus no new matter is added.

The amendment to claim 24 addresses the Examiner's rejection under 35 U.S.C. § 112 by clarifying who the recipient in the claimed method is. The amendment also addresses the Examiner's rejection based on anticipation by Pines (U. S. Patent 5,449,678; hereinafter, "the '678 patent").

The Examiner asserts that the '678 patent teaches the use of quinazolinone for treating or preventing fibrotic disorders, citing col. 6 line 4. Applicants respectfully disagree. The '678 patent discloses treatment, but not prevention of fibrotic disorders. The disclosure of the '678 patent states that the invention therein provides compositions and methods for "treatment of post-inflammatory fibrosis, such as myocardial fibrosis". Col. 6, line 3-4. Moreover, the claims of the '678 patent recite a "method for treatment of a fibrotic condition [in a] human patient suffering therefrom" (claim 1) and a "method for treating a disease state associated with excessive collagen deposition in a human patient" (claim 6).

In contrast, claim 24, as amended, is directed to preventing the development of a fibrotic condition in heart tissue of patients who are at risk for fibrotic diseases because they are exposed to promoters of cardiac fibrosis. These fibrogenic conditions may include tissue trauma or a mechanistically related process, as described in the application. See e.g., p. 12, line 15- page 13, line 2.

Prevention of the development of fibrosis is, moreover, demonstrated in Example 5, p.27, lines 20-28, wherein the simultaneous administration to a rat of a promoter of cardiac fibrosis, angiotensin II, with halofuginone, prevented a change in collagen volume, an increase in collagen volume causing the fibrotic condition. Thus, the administration of halofuginone in this experiment was to prevent the development of a fibrotic condition and not for treatment of a fibrotic condition. Accordingly, the '678 patent neither discloses nor suggests the subject matter of the amended claims.

Applicants believe that the amendments presented herein place the application in condition for allowance. Accordingly, applicants respectfully request that the Examiner enter the claim amendments presented

herein, consider the foregoing remarks and allow the pending claims.

Respectfully submitted,



BEST AVAILABLE COPY

Jane T. Gunnison (Reg. No. 38,479)
Barbara A. Ruskin (Reg. No. 39,350)
Shilpi Banerjee (Reg. No. 53,965)

Attorneys for Applicants

FISH & NEAVE
Customer No. 1473
1251 Avenue of the Americas
New York, New York 10020-1105
Tel.: (212) 596-9000
Fax: (212) 596-9090